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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,691	02/25/2002	Stephen Donovan	D-3018	5311

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EXAMINER	
MARX, IRENE	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,691	DONOVAN, STEPHEN	
	Examiner	Art Unit	
	Irene Marx	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,12,17-19 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 12, 17-19, 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/10/04 has been entered.

Claims 1-8, 12, 17-19, 22-26 are being considered on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-8, 12, 17-19, 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that neither the botulinum toxin component nor the substance P component required to be covalently coupled for effectiveness for the intended purpose of "treating neurogenic pain" is claim designated. It is not apparent that any "component" regardless of size will have the required effect . While some of the dependent claims define one of the components, in none of the dependent claims are both components to be covalently coupled properly defined.

Claim 19 is vague and indefinite in that the mode of administration intended by "systemically" is not ascertainable.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 12, 17-19, 22-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of arthritis pain by administration of an

agent of a botulinum toxin (BT) component covalently coupled to substance P, wherein the botulinum toxin component is the proteolytic domain (L chain) or the peptide of proteolytic domain and the translocation domain of a BT (LH_N), composition as claimed by intravenous route, does not reasonably provide enablement for a method of treating any neurogenic pain in a subject wherein the agent comprises a botulinum toxin component covalently couple to a substance P component and its administration is by any route whatsoever, including orally and "systemically". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

From the record of the present written disclosure it is apparent that treatments were conducted with specific preparations administered in a specific manner. Specification, pages 31-39, wherein administration and treatment is reported.

The factors to be considered in determining whether undue experimentation is required are summarized in In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a prima facie case.

(1) The breadth of the claims.

The claims are broad and encompass unspecified variants of the botulinum toxin component, including small fragments, including some wherein the H_C of the neurotoxin is mutated or modified to reduce its ability to bind to the receptors at the neuromuscular joint as well as an undefined substance P component.

The breath of the claims is such that it encompasses just a few amino acids as "components". Neither the botulinum toxin component nor the substance P component required to be covalently coupled for effectiveness for the intended purpose of "treating neurogenic pain" is claim designated in a single claim. It is not apparent that any "component" regardless of size

will have the required effect, such as a component comprising two or just a few random amino acids. .

(2) Working examples

There are no working examples of the claimed method in association with components of the botulinum toxin other than LH_M and substance P itself.

(3) State of the art

The general knowledge and level of skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on treating conditions using an agent of a botulinum toxin component and a substance P component, wherein the botulinum toxin component contains a modified H_C to be fully enabled.

(4) Predictability of the art and Nature of the invention

The nature of the invention encompasses therapy. Pharmaceutical therapies are unpredictable for the following reasons: (1) therapeutic compositions may be inactivated before producing an effect, i.e. such as proteolytic degradation of the peptide or protein; (2) the therapeutic composition may not reach the target area, I. e. the peptide or protein may not be able to cross the mucosa or may be adsorbed by fluids, cells and tissues where the peptide or protein has no effect, (3) other functional properties, known or unknown, may make the therapeutic composition unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. App. & Inter. 1992).

Also the characterization of arthritis as a neurogenic disease is queried. The dictionary definition (*The American Heritage ® Dictionary of the English Language, Fourth Edition* Copyright © 2000 by Houghton Mifflin Company) of neurogenic is defined as:

"Originating in the nerves or nervous tissue: *a neurogenic tumor* or Caused or affected by the nerves or nervous system: *neurogenic disorders*". See, also specification, page 11, lines 27-31.

Arthritis is defined as:

"Inflammation of a joint, usually accompanied by pain, swelling, and stiffness, and resulting from infection, trauma, degenerative changes, metabolic disturbances, or other causes. It occurs in various forms, such as bacterial arthritis, osteoarthritis, or rheumatoid arthritis."

Thus, although arthritis is related to inflammation pain, there is no clear indication that the affliction involves "neurogenic inflammation pain". At Specification, page 15, lines 19-20, it is stated that "certain forms of arthritis" may be included under "neurogenic inflammation". However, this does not constitute a proper definition of the disease intended. It is noted that in the Examples the nature or diagnostic basis for the indication of "neurogenic inflammation pain" in selected patients is not set forth. Moreover, for the treatment of rheumatoid arthritis the treatment is injection of about 1 to about 50 units of a specific botulinum toxin - substance P conjugate into or near the region of pain.

Thus given high level of unpredictability in the art one of ordinary skill in the art at the time of the invention would require a substantial inventive contribution to practice the invention, especially with its current breadth. Moreover, the narrow working embodiments in the examples can not be a sole factor in determining enablement. However its limited showing, in light of the unpredictable nature of the art and the lack of direction provided by the applicant presents, provides additional weight to the lack of enablement in consideration of the Wands factors as a whole. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention.

Therefore, the scope of the claims is not commensurate with the teachings of enablement of the specification.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (571) 272-0919. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 .

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Irene Marx
Primary Examiner
Art Unit 1651